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ABSTRACT

This invention provides methods for modifying a selected gene in cells of a mammalian skin at one or more locations by delivering to the skin cells an effective amount of a composition having a chimeric RNA-DNA oligonucleotide for causing heritable modifications in the selected gene so that the heritable modifications result in phenotypic changes at the locations of the mammalian skin. The invention specifically provides a method for permanent gene correction of a gene mutation by an RNA-DNA oligonucleotide (RDO) *in vivo*. By this method, a point mutation in the albino BALB/c mouse tyrosinase gene *in vivo* has been corrected thereby providing for permanent and inheritable restoration of tyrosinase enzymatic activity, melanin synthesis, and pigmentation changes in melanocytes of skin at the treated locations. Both topical application and intradermal injection of this oligonucleotide to mice skin resulted in dark pigmentation of several hairs in localized area.